polyposis and Gardner syndrome.[7] The general age range is 6 months to 12 years.

The hyperplasia is characterized radiologically by small, relatively uniform, umbilicated polypoid lesions, involving all or part of the large intestine. Unique for lymphoid hyperplasia is the presence of a small amount of barium in the center of the polyps; that is, an umbilication at the apex of the lymphoid nodule.[1] This umbilication has *not* been observed in multiple polyposis or juvenile polyps of the large intestine.[1]

Histologically, the submucosal nodules are composed of lymphoid follicles within the normal mucosal pattern. The follicles consist of mature lymphocytes and reticulum cells with or without germinal centers.[8]

The symptomatology in this condition has included vague abdominal pain, sporadic or recurrent (40 to 80 percent), rectal bleeding (0 to 70 percent), constipation or diarrhea (10 to 40 percent).[1,3,9] The rectal bleeding has been microscopic as well as macroscopic in nature and may be persistent. Anemia is usually not present. There are no specific laboratory studies.

Because of the earlier confusion with multiple polyposis of the colon, treatment has included radiation therapy or colectomy, as well as prolonged corticosteroid administration.[1] When lymphoid hyperplasia has been diagnosed, no specific treatment is indicated since a spontaneous regression usually occurs within months.[1,3] If the rectal bleeding persists or if severe abdominal pain occurs in this condition, treatment with corticosteroids (prednisone) can be instituted for two to four weeks.

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Cerebral Abscesses Complicating Neonatal Citrobacter freundii Meningitis

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THE CITROBACTER GENUS of bacteria, although once regarded as nonpathogenic, has been responsible for many well-documented pathologic conditions, especially in compromised hosts. These include urinary tract, pulmonary and bone infections;[1] gastroenteritis;[2] gangrenous ulcer with septicemia,[3] perinephric abscess[4] and meningitis.[5-10] Species of Citrobacter are still a rare cause of meningitis, but several reports have appeared in recent years implicating this group of organisms as the cause of neonatal meningitis with high morbidity and mortality. Development of a cerebral abscess complicating meningitis due to Citrobacter freundii has been reported before but without specific bacterial documentation. In this report, we provide bacteriologic and pathologic confirmation of this uncommon but devastating complication.

Report of a Case

A white infant girl was transferred to Harbor General Hospital at the age of six weeks for evaluation and treatment of intractable Citrobacter freundii meningitis.

The infant was born to a 24-year-old primipara following a normal term pregnancy and delivery. Birth weight was 3.1 kg (6.8 pounds). The

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infant went home on the third day, where she ate poorly and was lethargic; her crying was reported to be weak. On the fifth day, fever and a bulging fontanelle were noted. That evening right-sided clonic seizures occurred and the infant was admitted to the referring hospital.

On admission, temperature was 99.6°F (37.6°C), respirations 40 per minute, and a pulse rate of 140 beats per minute. Head circumference was 33.5 cm, and the fontanelle was bulging. There were right-sided clonic seizures with ocular deviation to the right. The neck was supple. Muscle tone was generally increased, but no paralysis was noted. Grasp and Moro reflexes were good.

Initial laboratory findings were as follows: Hemoglobin value was 14.2 grams per 100 ml and leukocyte count was 20,700 per cu mm with 59 percent polymorphonuclear leukocytes (PMN), 16 percent lymphocytes, 20 percent monocytes, 4 percent myelocytes and 1 percent eosinophils. Lumbar puncture showed grossly turbid cerebrospinal fluid (CSF). CSF cell count was 17 red cells per cu mm and 1,490 leukocytes per cu mm of which 88 percent were PMN. CSF glucose was 40 mg per 100 ml and total protein was 838 mg per 100 ml. No organisms were seen on stained smear.

The infant was immediately started on a regimen of ampicillin, 200 mg per kg of body weight per day given intravenously, and kanamycin, 15 mg per kg per day given intramuscularly, which led to some clinical improvement but without decrease in the CSF cell count. Citrobacter freundii was cultured from the CSF and was found to be resistant to ampicillin. Therapy was then started with cephalothin, 100 mg per kg of body weight per day given intravenously, again without decrease in the CSF cell count. Over the following three weeks the patient received gentamicin given intravenously and intrathecally, chloramphenicol given intravenously, and a second course of ampicillin, all of which failed to clear the CSF of inflammatory cells.

On transfer to Harbor General Hospital, the infant was irritable and had opisthotonos. The pulse rate was 164 beats per minute, respirations 60 per minute and temperature 102.2°F (39°C). Head circumference was 37.5 cm. The fontanelle was full, and there was nuchal rigidity. Liver was palpable 3 to 4 cm below the right costal margin, but the remainder of the general examination findings were within normal limits. Cranial nerves were intact. There was generalized increase in tone and hyperreflexia. Right-sided decorticate posturing was observed, but a Moro response was symmetrical. Head control, sucking and grasp reflexes were poor.

A lumbar puncture was traumatic, but the CSF glucose value was 24 mg per 100 ml and total protein 266 mg per 100 ml. No organisms were seen on smear, and cultures showed no growth. Serum immunoglobulin levels were as follows: IgA, 32 mg per dl (normal, 4 to 36 mg per 100 ml); IgG, 275 mg per dl (normal 200 to 950 mg per 100 ml); IgM, 125 mg per dl (normal, 20 to 80 mg per 100 ml), and IgD, 0 (normal, 0 to 6 mg per 100 ml). Chest and skull x-rays were normal. An electroencephalogram showed diffuse slowing with epileptogenic foci in the left parietal, left temporal and right parietal regions. A brain scan with Technetium 99m (^{99m}Tc) pertechnitate showed a large "cold" area within an area of increased uptake in the left posterior parietal region consistent with an abscess. Two other smaller areas in the left temporal and right parietal regions were also considered suspicious. Subdural taps were dry. Cerebral angiography showed findings consistent with hydrocephalus but without definite mass effect.

The infant was continued on chloramphenicol therapy, 100 mg per kg of body weight per day given intravenously. Following angiography, frequent seizures were noted which responded poorly to large doses of anticonvulsant medications. In view of the hydrocephalus, an external ventricular shunt with a low pressure Holter valve was placed, but the infant's condition continued to deteriorate. She died at the age of 7½ weeks.

Bacterial Isolation

Three CSF specimens and a ventricular fluid specimen were submitted for culture. Citrobacter freundii was recovered from all specimens using sheep blood and chocolate agar plates for primary isolation. The Gram-negative organism was identified using the differential media, R/B, of General Diagnostics, Inc. Negative reactions recorded were phenylalanine deaminase, indole, lysine decarboxylase, ornithine decarboxylase and raffinose. Positive reactions were hydrogen sulfide production, gas from glucose fermentation, motility, citrate utilization, lactose, rhamnose, sorbitol and arabinose fermentation.

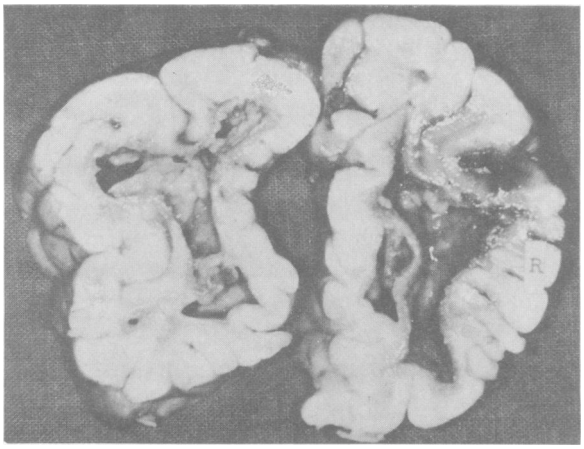

Figure 1.—Coronal section through the posterior parietal lobes showing bilateral abscesses.

Autopsy Findings

General autopsy findings included focal, healed pneumonitis; mild, focal, chronic pancreatitis; acute and chronic passive congestion of the liver, spleen, and adrenal glands; mild, focal, adrenal cortical nodular hyperplasia, and stress ulcers of the stomach.

The brain weighed 470 grams and showed moderate flattening of the gyral surfaces and focal areas of softening of the parietal lobe convexities on both sides. Approximately 25 ml of greenish, purulent material escaped from a cortical defect created through an area of softening in the left parietal lobe. Leptomeninges were cloudy over the convexities and thickened and opaque over the ventral aspect of the brain stem. Sections showed the presence of three separate large abscesses filled with yellowish, purulent exudate—one occupying the frontal white matter, anterolateral to the anterior horn of the left lateral ventricle; a second largely replacing the white matter of the left parieto-occipital lobe with ventromedial displacement of the posterior horn of the lateral ventricle, and a third abscess occupying a similar position as the second but on the right side (Figure 1). Traces of purulent exudate were found throughout the lateral and third ventricles, and the fourth ventricle was nearly filled. The aqueduct of Sylvius was grossly occluded at its midpoint.

Studied microscopically, the abscesses were shown to be chronic with a content of necrotic debris and persistent acute inflammatory cells and a wall of a relatively wide zone of granulation tissue with prominent neovascularization surrounded by an atypically wide zone of astrogliosis (Figure 2). In the latter zone, the astrocytes were rather numerous and hypertrophied. In other areas, the cerebral white matter showed diffuse astrogliosis, especially where white matter faced the ventricles. Rare, small foci of noninflammatory necrosis were noted, some with calcification. Leptomeninges were mildly fibrotic and the spaces contained sparse inflammatory cells. The ependyma of the lateral ventricles was greatly attenuated in areas, and the ventricles contained cellular debris and polymorphonuclear leukocytes. The cerebral cortex was intact for the most part except where the abscess approached the surface.

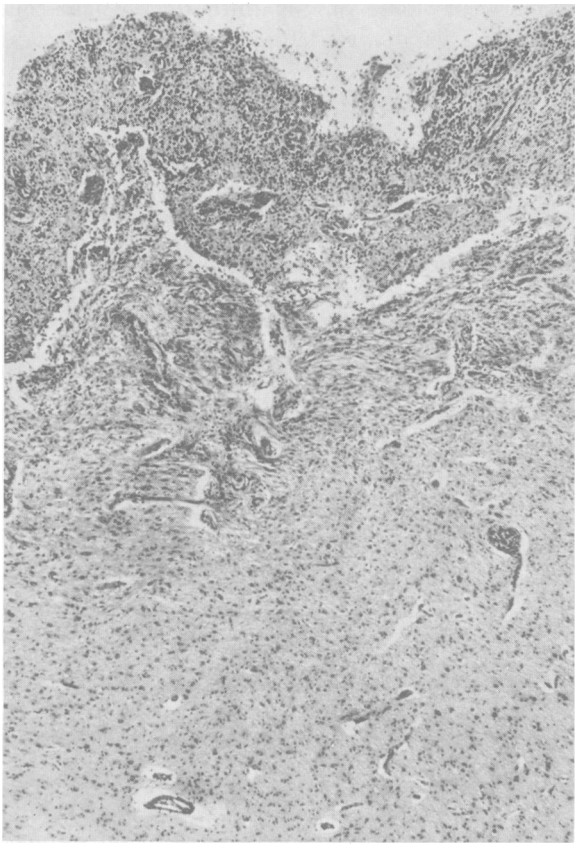

Figure 2.—Photomicrographs of abscess wall consisting of layers of inflammatory cells, zone of granulation tissue, and a wide zone of astrogliosis extending into surrounding white matter. (H and E × 42)

Comment

The classification of Bacterium freundii has been controversial since it was first isolated in 1928.[11] The organism has been reclassified variously as Citrobacter freundii, Escherichia freundii, Colobactrum freundii and Paracolobactrum freundii.[12] The accepted name today is Citrobacter

freundii, but biochemically closely related microorganisms such as Escherichia intermedium and the Bethesda-Ballerup group have been assimilated into this genus. The genus is therefore heterogeneous, and at least two species exist by current classifications: C. freundii and C. diversus.[13] C. diversus is considered to be heterogenous by some investigators and has been divided into C. koseri and a new genus, Padlewski or Levinea. The eighth edition of *Bergey's Manual of Determinative Bacteriology* speciates Citrobacter into C. freundii and two biotypes (a and b), or C. intermedius which is synonymous with Padlewski or Levinea and C. koseri, respectively.[11]

A review of 13 cases of Citrobacter meningitis from the literature (Table 1) shows the following: 6 of 9 cases were males; 10 of 13 infants were either premature or of low birth weight; 10 of 13 had symptoms before 14 days of age, and, in general, the prognosis conformed to the universally poor statistics for neonatal meningitis with mortality approaching 50 percent and neurologic residua in 40 percent. Cerebral abscesses were reported to have occurred in at least two of the cases but are incomplete in details.

The diagnosis of this disease, as in all neonatal meningitides, was difficult. There is no characteristic clinical constellation of signs and only a high index of suspicion in a premature infant with vague symptoms may establish an early diagnosis. Radioisotope brain scan, as shown in this report, is a valuable tool and may be more sensitive than angiography in confirming the diagnosis of cerebral abscess.[14] The treatment of choice is a combination of prolonged parenteral antibiotic treat-

TABLE 1.—*Review of Cases of Citrobacter Meningitis*

Author(s)	*Age (Days)*	*Sex*	*Gestation/Weight (Week) (Grams)*	*Organism*	*Course*	*Postmortem Findings*
Harris and Cone[5] 1960	49	♀	Term/—	E. freundii*	Seizures, hydrocephalus, psychomotor retardation, and rigidity	..
	2	♂	36/2,250	E. freundii*	Died	Acute leptomeningitis with abscess of the right cerebrum
Shortland-Webb[6] 1968	35	♂	32/1,800	C. freundii	Died	Purulent exudate covered the cerebellum and both cerebral hemispheres
Cavalieri and Piacentini[7] 1968 ..	4	♂	Term/3,500	C. freundii	Aqueductal stenosis with hydrocephalus	..
Gwynn and George[8] 1973	4	♂	33/2,000	C. koseri	Died	Widespread necrosis of right hemisphere with meningeal congestion and base exudate
	6	♀	Twin pregnancy	C. koseri	Superficial brain abscess, subdural empyema, hydrocephalus, and porencephalic cysts	..
	13	♂	Term/1,720	C. koseri	No sequelae	..
	9	♂	32/1,820	C. koseri	Hydrocephalus with extraventricular cystic cavities and subdural empyema	
Gross et al[9] 1973	<7	?	Premature	C. koseri	Died	No postmortem examination done
	<7	?	Premature	C. koseri	Died	No postmortem examination done
	<7	?	Premature	C. koseri	No sequelae	..
	7	?	37/—	C. koseri	No data	..
Tamborlane and Soto[10] 1975 ...	42	♀	38/2,532	C. diversus	Aqueductal stenosis with hydrocephalus	..
Present case	6	♀	Term/3,100	C. freundii	Died	See text for postmortem findings

*Escherichia freundii—former classification of Citrobacter freundii

ment and early surgical management of neurologic complications.

The patient of this report was somewhat unusual in that she was born following a term pregnancy, birth weight and delivery were normal, and there were no predisposing obstetrical complications. There was no evidence of underlying cardiac or other disease, and the infant was immunologically intact. We conclude, as others have, that not all infections due to the Citrobacter group of organisms represent opportunistic infections in a host with compromised resistance, but rather that the Citrobacter group should be regarded as important pathogenetic organisms.

Summary

Bacterial meningitis developed in an infant during the neonatal period. Failure to respond to aggressive antibiotic therapy was shown at postmortem examination to be due to multiple brain abscesses. The causative organism was proved to be Citrobacter freundii.

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Luring the Husband to Participate in Marital Counseling

If a marriage is troubled enough to involve both husband and wife in counseling, then you must lure him in. It's usually the husband who does not want to come in. And if she says, "Well, I know darned well he won't come in," then the trick, which works for almost all cases, is for you to intercede in the following fashion. . . . Call him up and say something like, "I saw your wife yesterday in the office. I think she's got some problems I should talk to you about." . . . And things like, "Well, I'll tell you. I know your wife and she hasn't been quite her smiling happy self lately and I know you'd like to change that. And I think you can help her out. So come in at such-and-such a time and we'll talk it over."

—BEVERLEY T. MEAD, MD, *Omaha*
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